20. The method of claim 14 further comprising the step of binding a carbohydrate or derivative thereof to the organic group.

21. A method to bind a carbohydrate or a derivative thereof to a gold surface, comprising:

coating the gold surface with a thiol compound which contains an organic group and

binding a carbohydrate or derivative thereof to the organic group.--

REMARKS

Reconsideration is respectfully requested of the Official Action of February 12, 1997 relating to the above-identified application.

In the Office Action of February 12, 1997, the Examiner objected to the disclosure due to the misspelling of the words; "specifically" and "aliphatic" and also because the abbreviation "SPDP" was not completely spelled out. These informalities have been corrected by the above amendments to the specification. Applicants thank the Examiner for pointing out these informalities and, in light of the amendments, request withdrawal of the objection.

The Examiner rejected claims 1-16 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 1 is indefinite because it is unclear where and by what a protein is to be bound.

Claim 1 has now been amended to definitely state that the carbohydrate derivative is bound to a surface of the biosensor and also binds a protein, cell or virus.

Claims 6 and 7 were rejected due to lack of antecedent support for the recitation of "the aglycon part" in claim 1.

Claim 1 has now been amended to definitely recite "an aglycon part".

Claims 8, 9 and 13 were rejected as allegedly being vague and indefinite with respect to the recitation of "said surface" because it is unclear if it is the surface where the carbohydrate derivative is bound or another surface of the biosensor.

Claim 8 recites a surface which has been definitely claimed in claim 1, as discussed above, and upon which claim 8 is dependent. Claim 9 has been amended to indicate that the binding of a protein, virus or cell is to the carbohydrate derivative that is bound to the surface of the biosensor.

Claim 9 was rejected as allegedly being indefinite with

respect to the recitation of "at the binding".

Claim 9 has now been amended to recite "upon binding" as the Examiner suggested in the Office Action.

Claim 14 was objected to because of the recitation of unconventional claim language.

Claim 14 has been amended to change "characterized" to "where in" as the Examiner suggested in the Office Action.

Claim 15 was rejected with respect to the recitation of the term "modified" because it is alleged that it is unclear how the surface is modified.

Claim 15 has been amended to definitely state that the aglycon part of the carbohydrate molecule is covalently bound to the gold surface of the biosensor.

Claim 16 was rejected because it allegedly did not set for any process steps. Claim 16 was also rejected under 35 U.S.C. § 101 for the same reason.

Claim 16 has now been amended to definitely recite the steps of exposing the biosensor to a sample and measuring or detecting a protein, virus or cell.

The Applicants thank the Examiner for his helpful suggestions regarding amendments to claims 1-16. Applicants submit that, as amended, claims 1-16 are definite and particularly point out and distinctly claim the subject matter

which Applicants regard as the invention and furthermore properly define a process. Accordingly, Applicants respectfully traverse the rejection and request reconsideration.

The Examiner rejected claims 1, 2, 9, 10, 15 and 16 under 35 U.S.C. § 102(b) as being anticipated by Attridge et al., (WO 90/01166) for the reasons of record in the previous Office Action (paper no. 8).

Applicants respectfully traverse the rejection and request reconsideration.

Claims 2, 9, 10, 15, and 16 depend from claim 1 or utilize the biosensor defined in claim 1. Claim 1, as amended, describes a biosensor on which is bound a carbohydrate derivative with an aglycon part. The aglycon part of the carbohydrate derivative is included to provide unique and beneficial properties to the claimed biosensor as described in the specification on page 4, line 29, through page 5, line 9.

Attridge et al., teach specific carbohydrates as binding partners for the sensor. Carbohydrate derivatives and aglycon parts of the carbohydrate derivatives are not taught by Attridge et al. Accordingly, claims 1, 2, 9, 10, 15 and 16 describe a unique biosensor unanticipated by Attridge.

The Examiner rejected claims 1, 2, 11, and 16 under 35 U.S.C. § 103(b) as being anticipated by Karube (EP 0 215 669) for the reasons of record in the previous Office Action (paper no. 8).

Applicants respectfully traverse the rejection and request reconsideration.

Claims 2, 11 and 16 depend from claim 1 or utilize the biosensor defined in claim 1. Claim 1, as amended, describes a biosensor on which is bound a carbohydrate derivative with an aglycon part. Karube discloses only sugars as a carbohydrate for use as a binding partner. As discussed above, derivatized carbohydrates and the aglycon part of the biosensor are unique features undisclosed by Karube. Accordingly, claims 1, 2, 11 and 16 describe a unique biosensor unanticipated by Karube.

The Examiner rejected claims 3-8 and 12-13 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Attridge et al., in view of Nilsson et al., (US Patent No. 4,918,009 (hereinafter '009)) for reasons of record in the prior Office Action (paper no. 8). In the prior Office Action of April 28, 1996, the Examiner stated that:

> Attridge et al., disclose a biosensor comprising a gold surface-immobilized carbohydrate for detecting a protein, virus or cell... Attridge et al., teach that

specific carbohydrates may be used as the biosensor receptor to bind lectins specific for the carbohydrate. ...Nilsson et al., teach that many of the carbohydrate derivatives are specific for various bacterial lectins and suggest their use in diagnostics and that they may be immobilized on solid carriers.

The Examiner has stated that the carbohydrate bound to a solid phase taught by Nilsson et al., is seen to be functionally equivalent with the biosensor surface of Attridge et al.

Applicants note that Nilsson et al., '009 do teach carbohydrate derivatives which can be bound on solid surfaces for use in such applications as affinity chromatography and that Attridge et al., do teach specific carbohydrates for use with their sensor. However, Applicants have discovered that carbohydrate derivatives with an aglycon portion of the molecule can be uniquely selected for use in biosensor applications so as to modify the binding affinity of the carbohydrate derivative for its corresponding binding ligand by reducing steric hindrance of the bound carbohydrate derivative. Examples of the carbohydrate-R-X-biosensor surface and carbohydrate-R-X-protein-biosensor surface are given as spacer configurations for modifying carbohydrate steric hindrance (page 5, last line, to page 6, line 14). This manner of controlling biosensor analyte binding affinity has not been

taught or suggested by either Attridge et al. or Nilsson et al., '009. The aglycon part used for both binding the carbohydrate derivative to the biosensor surface and for adjusting the binding parameters by controlling the steric hindrance is present in claim 1 and therefore is descriptive of the biosensor of claims 3-8 and 12-13 which depend from claim 1.

Applicants submit that the formation of a biosensor comprising a carbohydrate derivative bound via an aglycon part to the surface of the biosensor has not been taught or suggested by either Nilsson et al., '009 or by Attridge et al. The use of this configuration solves the problem of stericaly hindered carbohydrate derivatives on the biosensor surface. Furthermore, neither Attridge et al., or Nilsson et al., '009 identified this problem which is solved by the present invention. The problem faced by the Applicant and the solution to the problem must be considered in the criteria for testing for obviousness under 35 U.S.C. § 103. It is settled that:

> [Where] there is no evidence of record that a person of ordinary skill in the art at the time of [an applicant's] invention would have expected [a problem], ...it is not proper to conclude that [an invention], which solves this problem ...would have been obvious to that hypothetical person of ordinary skill in the art. *In re Nomiya*, 184

USPQ 612 (CCPA 1975).

The prior art reference must elucidate the problem when it is being cited for making the solution obvious.

The Applicants submit that 3-8 and 12-13 describe biosensors which are based on the biosensor described in claim 1. The biosensor of claim 1 comprises a solid surface to which a carbohydrate derivative with an aglycon part is bound through the aglycon part of the molecule. This unique construction imparts the flexibility to reduce steric hindrance of ligand-substrate binding thus improving performance. This type of configuration in a biosensor application has not be taught or suggested by Nilsson et al., '009 or by Attridge et al.

Therefore, the Applicants respectfully traverse the rejection of claims 3-8 and 11-12, and respectfully request reconsideration.

The Examiner rejected claim 14 under 35 U.S.C. § 103(a) as being unpatentable over Attridge et al., for reasons of record in the prior Office Action (paper no. 8). In that Office Action, the Examiner stated that Attridge et al. teach functionalizing the gold surface in order to facilitate coupling of the ligand to the gold surface with a thiol compound. The Examiner further asserts that the techniques to accomplish such coupling are well known in the art and the

Examiner references the instant specification at page 5, 4th paragraph, as an admission of the prevalence of such knowledge.

Applicants respectfully call to the Examiner's attention that Attridge et al. describe the functionalizing of a silica surface at the above-cited location in the Attridge et al., reference. Additionally, the cited passage in the Nilsson et al., specification refers to prior art modification of functional groups pre-existing on solid supports not the modification of a gold surface and the subsequent coupling of a carbohydrate derivative via an aglycon part. The teaching of gold surface modification and coupling comes only from the instant specification.

Applicants submit that Attridge et al. is entirely silent on any method of covalently coupling ligand to a gold biosensor surface. Furthermore, the method described in the instant specification and claimed in claim 14 is not a technique known in the art or an obvious modification thereof. Accordingly, Applicants respectfully traverse the rejection of claim 14 and request reconsideration.

The new claims 17-19 are dependent on claim 1 and are further descriptions of the Applicants' immobilized carbohydrate biosensor. Support for claim 17 comes from page 4, 4th paragraph et seq. Support for claims 18 and 19 is found

on page 5, last line, to page 6, line 14. Claim 20 is a further description of the method of claim 14. Claim 21 is a method of binding a carbohydrate or carbohydrate derivative to a gold surface as disclosed in the specification and Example. Claims 17-21 are added to more adequately describe the invention of the Applicants.

In light of the foregoing, Applicants submit that the claims, as amended, definitely and distinctly claim the Applicants' immobilized carbohydrate biosensor. Furthermore, the Applicants' invention is neither anticipated by or obvious under the cited prior art. Therefore, Applicants respectfully request favorable action in the form of allowance of the claims at the Examiner's earliest convenience.

Respectfully submitted,

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